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Pamela F. Herbert

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PERCUTANEOUS ELECTRICAL STIMULATION AND THE THRESHOLD FOR LIGHT TOUCH

Pamela F. Herbert

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fulfillment of the requirements
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"But all these requisites belong of old to medicine, and an origin and way have been found out, by which many and elegant discoveries have been made, during a length of time, and others will yet be found out, if a person possessed of the proper ability, and knowing those discoveries which have been made should proceed from them to prosecute his investigations."

Hippocrates
"On Ancient Medicine"

ABSTRACT

The digital nerves of human subjects were stimulated with continuous .1 ms square wave direct current pulses at 1 and 100 Hz and 4-50 volts and the effect on digital thresholds to light touch and on initiation and conduction of the median nerve action potential was studied.

In the first experiment, stimulation for 25 minutes with D.C. current pulses of .1 ms, 100 Hz, 30 v resulted in elevation of the threshold to light touch distal to the electrodes in the stimulated finger. The high frequency stimulation also resulted in an inconstant depression of the median nerve action potential, the amplitude of which was not related to increases in touch threshold. Neither of these effects were seen with .1 ms, 30 v pulses at 1 Hz.

In the second experiment subjects were stimulated for 15 minutes with .1 ms, 100 Hz pulses at a voltage just below their sensory threshold to the electrical stimulation. Subjects did not experience elevation of threshold to light touch.

In the third experiment, subjects were stimulated with .1 ms, 100 Hz currents at a voltage sufficient to produce a predetermined elevation of threshold to light touch and the effect was studied over a period of twenty minutes. There was no consistent or significant change in the elevation of touch threshold once the predetermined level had been reached.

After cessation of current, thresholds returned to control levels in 5 seconds or less in all subjects. In no experiment was an increase of threshold to light touch detected proximal to the electrodes on the stimulated finger or on any part of adjacent fingers.

On the basis of results of these and other experiments, a hypothesis is offered for the mechanism of the observed elevation of touch thresholds with electrical stimulation based on block of transmission of impulses from the receptor to the primary afferent axon.

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THEORETICAL FRAMEWORK

Theories of Cutaneous Sensation

Theories of cutaneous sensation can be divided into two groups: Specificity theories and pattern theories. The first modern specificity theory was proposed by Mueller in 1842 and was called the doctrine of specific nerve energies. Mueller hypothesized that the five Aristotelian senses of sight, hearing, smell, taste, and touch were transmitted to the brain by five different kinds of sensory nerve (Sinclair, 1967). Studies in the late 19th and early 20th century showed that nerve impulses are essentially the same in all sensory nerves, shifting attention away from Mueller's theory and toward a theory based on specific cutaneous receptors.

Investigation of cutaneous sensation led to the division of the Aristotelian sense of touch into four cutaneous "modalities": Touch, warm, cold and pain sense (Sinclair, 1967). Descriptions by Krause, Ruffini, and Meissner of specialized nervous structures in the skin, joints, and mesenteries lead Von Frey in 1895 to propose his theory of cutaneous sensation. Von Frey correlated the location of these new receptors on the human body with maps of maximum sensitivity to the four cutaneous modalities of sensation. For example, since Meissner corpuscles are frequently found on the fingers and palm of the hand where spots in the skin sensitive to touch are also most abundant, Von Frey concluded that Meissner's corpuscles were touch

receptors. By a series of similar deductions he concluded that cold was perceived by Krause end organs, warm by Ruffini organs, and pain, being felt everywhere, was served by the ubiquitous free nerve endings.

Sherrington, in 1900, outlined the expected behavior of receptors specific for one modality of cutaneous sensation such as Von Frey hypothesized:

> The sensorial end-organ is an apparatus by which an afferent nerve fiber is rendered distinctively amenable to some particular physical agent, and at the same time rendered less amenable to i.e. is shielded from, other excitants. It lowers the value of the limen (threshold) of one particular kind of stimulus, it heightens the value of the limen of stimuli of other kinds (Sinclair, 1967).

Attempts to find receptors that fulfilled the requirements of Sherrington's definition failed to establish Krause and Ruffini organs as specific receptors. Until recently, only the Pacinian corpuscle, which responds to vibratory deformation of the skin at a threshold greatly below that of any other kind of stimulation fulfilled Sherrington's criterion. New instruments in recent years, by making it possible to record from single primary afferent fibers and from single receptors, have disclosed a new and varied group of receptors to specific kinds of touch and pressure stimuli. These will be discussed in a later section of this paper.

The second type of theory of cutaneous sensation is pattern theory. Impetus for the formulation of pattern theories came from the work of Naunyn (1889) on the pains of

tabes dorsalis. Successive brief applications of a warm test tube to the skin of a tabetic patient are at first felt only as warm, but then feel increasingly hot until the patient feels that his skin is being painfully burned (Melzack, 1973). A mechanism for temporal summation of nerve impulses in the central nervous system was proposed to explain this observation. The spatial and temporal patterns of nerve impulses determine the nature of sensation rather than separate modality-specific transmission routes. A much discussed modern pattern theory is the gate theory of Melzack and Wall (Melzack, 1973).

Recent studies suggest that modality-specific receptors transmit encoded information about the exact nature of a stimulus by means of pulse trains of impulses, as will be discussed below. Thus at the periphery, cutaneous stimuli are transduced by modality specific receptors, but codes of patterned nervous impulses are important in information transfer in the primary afferent axon and within the central nervous system (CNS).

Classification of Sensory Nerve Fibers

Cutaneous stimuli are transmitted to the central nervous system via myelinated primary afferent nerve fibers of various diameters and by small unmyelinated primary afferent nerve fibers. Each cutaneous nerve contains both unmyelinated and myelinated fibers in a ratio of about 4:1 respectively (Sinclair, 1967). The funiculi or bundles of nerve fibers

comprising the nerve are covered by a connective tissue sheath, the epineurium (Sinclair, 1967). Surrounding each funiculus is a sheath of collagenous and elastic tissue called the perineurium. The perineurium is continuous with the pia-arachnoid of the CNS (Shanthaveerappa and Bourne, 1963) and extends along the entire length of the nerve to terminate as the outer lamellae of the Pacinian corpuscle and other receptors (Krause, 1881), (Pease and Pallie, 1959). In myelinated fibers which have individual Schwann cell sheaths and end in receptor organs, the inner bulb of the receptor is derived from this Schwann sheath (Krause, 1881).

Unmyelinated fibers in peripheral nerves run in bundles of 15 to 20 fibers enclosed in the cytoplasm of a single common Schwann cell (Sinclair, 1967). Adjacent unmyelinated bundles regularly exchange axons along their course so that those fibers enclosed within a common Schwann sheath near the sensory ganglion are not necessarily the same fibers as those at the periphery (Cauna, 1973). In contrast, the myelinated fiber population within the funiculi of cutaneous nerves is identical throughout the length of the nerve.

The cell bodies of the primary afferent nerve fibers are the ganglion cells of the dorsal root. Each ganglion cell constitutes a sensory unit with a cutaneous field over which stimuli of the proper kind will cause discharge of the dorsal root ganglion cell. The area of the cutaneous

field will be dependent on the number and distribution of receptors that are innervated by the terminal ramifications of the primary afferent fiber. In some large myelinated fibers serving one specialized touch receptor, the cutaneous field may be only a millimeter square, while in some small unmyelinated fibers terminating by an arborizing pattern of free nerve endings, the cutaneous field may be a centimeter square. Cutaneous fields are characterized by various degrees of overlap with, and autonomy from, the cutaneous fields of other primary afferent fibers.

When primary afferent fibers subserving cutaneous sensation are classified according to diameter and conduction velocity, the two are found to vary directly.

TABLE I

Group	Diameter, micra	Conduction Velocity, m/s
Myelinated		
A-alpha	12-22	
A-beta	12-14	80-85
A-gamma	9-12	50-55
A-delta	1-9	25-30
Unmyelinated		
C		.25-3.0

Taking advantage of the observation that threshold to electrical excitation of a nerve fiber varies inversely with fiber diameter, Collins, Nulsen, and Randt (1960) stimulated fibers of the sural nerve with currents of increasing intensity in awake surgical patients. Stimulation of single

A-beta fibers was perceived by patients as a non-painful tap, throb or touch. Trains of stimuli were perceived as non-painful tingling and paresthesias in the cutaneous area of distribution of the nerve fibers stimulated. Inclusion of A-gamma fibers in the stimulus volleys produced similar sensations. Not until electrical stimuli were intense enough to include the smaller myelinated A-delta fibers were painful sensations perceived by the patients. Single stimuli were then felt as before but with a sharper quality while multiple stimuli gave rise to stinging, burning, or pricking pain. Finally when electrical stimuli to the sural nerve were intense enough to excite small unmyelinated C fibers single and multiple stimuli elicited pain whose quality was so unbearable that all patients refused to submit to further stimulation.

The results of this experiment suggest that larger A-beta and gamma fibers subserve some non-painful sensory modality and that A-delta and C fibers transmit sensations of pain. Although true of most fibers within each group, recent studies of C fiber mechanoreceptors show that there are some exceptions to this scheme.

Survey of Receptors to Touch

In 1716 Pacini described a structure in the deep dermis of the cat, and in 1741 this structure, now called the Pacinian corpuscle, was further described by Lehman (Pease and Quilliam, 1957). Better methods of staining in the 19th

century led to the description by Meissner, Krause and Ruffini of a varied array of similar small bodies associated with sensory nerves in epidermis, dermis, mesentery, muscle, and joints. At first these structures seemed to fall into four well-defined groups, Pacinian, Meissner, Krause, and Merkel organs, but as the number of different subtypes of the four groups of receptors grew the boundaries separating one type from another became fuzzy until, finally, Ruffini proposed that there were many intermediate forms of receptors and not just four simple types.

Miller, Ralston, and Kasahara (1958) have devised a simple morphological classification of the receptors that can be seen with silver stain and with methylene blue which divided them into three groups: free-endings, expanded tip, and encapsulated endings, and which can be arranged by appearance and location as follows:

> Free-endings: originate in dermal papillae and end between strata malpighii and strata spinosum and granulosum of epidermis.
> Expanded-tip: glabrous (hairless) skin-hederiform discs of Merkel: subpapillary dermis-Ruffini end organs; hairy skin-outer root sheath of hairs.
> Encapsulated endings: glabrous skin-Meissner's corpuscle; subpapillary dermis-Pacinian or Krause corpuscle; hairy skin-whole hair follicle enclosed in capsule.

Finally, a new population and classification of cutaneous mechanoreceptors has been defined on the basis of the discharge pattern of their primary afferent fibers upon

mechanical stimulation of their fine terminals or specialized end organs. These studies have led to the neurophysiological characterization of some of the classical receptors and has led to the discovery of new classes of mechanoreceptors that do not correspond to any in the old morphological classifications.

Three kinds of mechanoreceptors have emerged. Those specialized for: 1. position detection 2. velocity detection and 3. for the detection of rapid transients. One receptor can perform one or two of these functions (Burgess and Perl, 1973).

A position detector is defined as any receptor which discharges when a stimulator is stationary even when the afferent discharge ultimately adapts to zero. A static-displacement detector shows a non-adapting position response (Burgess and Perl, 1973).

A velocity detector is defined as a receptor whose frequency of discharge is related to the velocity of displacement (Brown and Iggo, 1967). Further, such a detector will generate impulses whose frequency plotted against increasing displacement will yield a horizontal line at constant velocity (Burgess and Perl, 1973).

Receptors specialized to detect rapid transients respond preferentially to rapid stimuli. They may be velocity detectors with a high velocity threshold or they may respond to the mathematical derivative of velocity, which is acceleration (Burgess and Perl, 1973).

Mechanoreceptors show other sources of variability. The characterization of any receptor must include the presence or absence of adaptation which is a decrease in firing over time during constant stimulation, and of fatigue which is a less vigorous response on repeated applications of the same stimulus. Some receptors show linear directionality, responding more vigorously to stimuli moving them in one direction than in another. Finally each receptor has a characteristic recovery cycle: exciting the receptor by two identical stimuli below a critical stimulus interval will result in an elevated threshold for the conditioned stimulus compared to the unconditioned one (Burgess and Perl, 1973).

With these principles in mind it is now possible to survey the mechanoreceptors in hairy skin, glabrous skin, and sinus hairs. Fig #1.

Mechanoreceptors in Hairy Skin

There are two mechanoreceptors in primate and feline hairy skin specialized to detect both position and velocity. They are designated Type I and Type II and their primary afferent axons are of the A-beta group. Type I mechanoreceptors were first identified by Iggo (1963), who described spherical domes in the epidermis, 150-250 micra in diameter, raised above the surrounding skin by about 100 micra. Fig #2. These domes seem to function as "touch spots". Recordings of nerve activity in fibers in the saphenous or sural nerve of cats showed that a 2-10 mg

stimulus applied vertically to a dome within the distribution of the nerve resulted in characteristic bursts of nerve impulses. The maximum frequency of the response was 1100 impulses/sec. It was slowly adapting, lasting for up to 30 min. (Iggo and Muir, 1969). The same stimulus applied 1 mm away from the dome, or movement of adjacent hairs did not result in impulse initiation.

The Type I receptors were found in a density of 10-20/cm square on the hind legs of cats (Iggo, 1963). Each dome is supplied by its own unbranched primary afferent axon. The axon upon entering the receptor in the deepest layer of the epidermis gives off 20-50 terminal branches each of which becomes associated with a specialized Merkel cell. The membranes of the terminal axon branch forming roughlv circular plates up to 10 micra in diameter and 1 micron thick. The Merkel cell membranes are closely apposed to these plates although the appositions do not have the structure of tight junctions (Iggo and Muir, 1969). The cytoplasm of the Merkel tactile cell near its apposition to the axon membrane has many dense osmiophilic granules which could be packets of a neurotransmitter chemical (Iggo and Muir, 1969). The cytoplasm of the Merkel cell is also rich in mitochondria. Perhaps, this is a specialization for maintained discharge, since rapidly-adapting receptors such as the Pacinian corpuscle have smaller numbers of mitochondria in comparable locations (Iggo and Muir, 1969).

Above the specialized Merkel cells is the epidermal dome. The Merkel cells are anchored to these cells by fine collaginous processes (Iggo and Muir, 1969) so that force applied to the epidermal dome is transmitted to the Merkel cells beneath.

The second mechanoreceptor in hairy skin specialized for both velocity and position detection is the Type II receptor. It was discovered by Iggo in 1966 (Burgess and Perl, 1973) and has been described in detail by Chambers, Andres, Duering, and Iggo (1972). The end organ of the Type II receptor is a Ruffini ending which is lightly encapsulated, situated in the dermis and supplied by one axon which bifurcates within the capsule to form a terminal arborization.

The receptors are spindle-shaped, oriented parallel to the long axis of the limb and measure 2.0-0.5 mm in length with a largest diameter of 50 micra in the equatorial area. The capsule arises from the perineural sheath of the afferent nerve fiber and has 4-5 layers of perineural cells forming lamellae. Fig #3.

The lamellated capsule surrounds a fluid-filled space. Within the fluid-filled space is an inner core composed of nerve terminals, connective tissue, and cells giving rise to membranes that divide the space around the core into compartments.

Type II receptor afferents always carry a resting

discharge and respond to vertical displacement of the skin over an area of 2.5 cm square with lowest threshold at skin directly overlying the Ruffini ending. Unlike Type I receptors, Type II receptors respond to directional stretching of the skin over an area of 25 square cm. Both Type I and Type II receptors have the property of linear directionality. They display their position and velocity responses only during movement away from the rest position i.e. downward vertical displacement (Burgess and Perl, 1973).

Although both Type I and Type II receptors detect velocity of deformation and amplitude of deformation (position), there are important differences between them. Fig #4. The Type I receptor is more sensitive to changes in velocity than to changes in position, while the reverse obtains in the Type II receptor. The Type I receptor responds to a constant stimulus with high frequency impulses (up to 1100 impulses/s) at regular intervals for the first 30 min. but then frequency drops and trains of impulses separated by exponentially widening intervals appear (Iggo and Muir, 1969). In contrast to the Type I receptor, the Type II receptor responds to a constant stimulus with a slower, regular train of impulses (Burgess and Perl, 1973).

The recovery time of these receptors is always the same whether they are stimulated by mechanical stimuli or by electrical impulses directed anti-dromically into the receptor. The Type I receptor has a shorter recovery cycle

than the Type II receptor. No depression of excitability is detected in the Type I receptor 40-50 ms after impulse initiation. If the receptor is stimulated at intervals of 10 ms, the threshold for impulse initiation is 1 1/2-2 times control values and the discharge pattern is more irregular (Burgess and Perl, 1973).

The Type II mechanoreceptor, on the other hand, shows decreased excitability for at least 100 ms after impulse initiation. When stimulated at 10 ms intervals, the threshold for discharge may be 3 times control values (Lindbloom, 1958).

To summarize the similarities between Type I and Type II mechanoreceptors: both detect position and velocity of deformation of the skin with a slowly-adapting response. They both are discharged by displacement of the skin 5-15 micra away from the rest position within a punctate field with a diameter of about 200 micra. The two mechanoreceptors differ in the following way: Type I receptors terminate in domes, while Type II receptors respond to stretching of a 25 sq. cm patch of skin overlying the receptor while Type I receptors show no stretch responses. Finally, Type II receptors tend to have a resting discharge, Type I receptors do not.

The second group of mechanoreceptors in hairy skin are those detecting velocity of displacement only. Of these, one group form the terminations of A-alpha fast-conducting

myelinated primary afferents, a second group are innervated by A-delta fibers, and a third form the endings of non-myelinated C fibers.

Of the velocity detectors innervated by A-alpha primary afferents, two further groups can be distinguished: receptors associated with hairs (3 subtypes), and receptors activated within cutaneous fields located between hairs (2 subtypes).

The hair receptors are associated with intermediate size hairs or guard hairs (Brown and Iggo, 1967). Each A-alpha fiber branches terminally around several follicles and each follicle gives rise to one hair. Displacement of any one hair causes a rapidly-adapting discharge volley in the primary afferent nerve. Displacement of a hair with constant velocity results in a regular afferent discharge obeying the law $R=KS^n$ where "R" equals the frequency of impulses in the response, "K" is a constant, "S" is a measure of stimulus velocity and "n" is an exponent less than 1. The uniform interspike interval at constant velocity of displacement, together with this power law relation between neural response and velocity of displacement indicates that frequency of discharge in rapidly-adapting hair follicle units could be used to transmit exact information about velocity of mechanical displacement of hair and skin (Brown and Iggo, 1967).

Three receptors having these characteristics of velocity

detectors innervate guard hairs. These are, in order of increasing threshold to velocity of displacement: G 2, intermediate, and G 1 receptors. The G 1 receptor has such a high threshold (20 mm/s displacement) that it also may be classed as a detector of rapid transients (Burgess and Perl, 1973), and will be discussed in the section dealing with detectors of rapid transients. The G 1 receptor innervates hairs over an area of 2.2-2.7 sq. cm, the intermediate hair receptor over an area of 1.4-2.3 cm and the G 2 receptor over an area of 0.7-0.9 sq. cm (Burgess, Howe, Lessler, and Whitehorn, 1974).

The receptors differ with respect to recovery cycle. G 2 hair receptors show decreased responses for up to 100 ms after impulse propagation. When stimulated at intervals of 10 ms, the threshold is found to be increased 2-2 1/2 times control values. The intermediate hair receptor has a shorter recovery cycle, showing no decrease in response 30-50 ms after a propagated potential.

The second group of receptors detecting velocity in hairy skin and innervated by A-alpha fibers are field receptors. These branch before terminating to supply an area of skin and do not respond to movements of isolated hairs (Burgess and Perl, 1973). Two types have been described, the F 1 receptor responding within an area of 2.0-2.5 sq. cm and the F 2 receptor with a cutaneous field of from 2.0-2.9 sq. cm (Burgess et al, 1974). The F 1

receptor has a velocity threshold and recovery cycle similar to the intermediate hair receptor (Burgess and Perl, 1973).

The second division of mechanoreceptors in hairy skin are innervated by A-delta fibers. Many of these receptors end on follicles which give rise to 2-4 small down hairs, others innervate guard hairs which arise singly from each follicle. Of all velocity receptors associated with hairs, down hair receptors have the lowest threshold to velocity of displacement (Brown and Iggo, 1967) and the smallest fields, 0.4-0.5 sq. cm (Burgess et al, 1974).

The third division of velocity detectors in hairy skin are innervated by slowly-conducting small unmyelinated C fibers. The frequency of impulses in the response is linearly related to the velocity of displacement in these receptors. The receptors require prolonged indentation of skin to discharge, 150-200 ms as compared to 3 ms in velocity detectors innervated by myelinated A fibers, so that they cannot signal rapidly changing stimuli. The precise time of onset of stimulation is obscured for them by the long minimal contact time required for their activation (Burgess and Perl, 1973). In addition, they respond with a slowly-adapting sustained discharge lasting at least 10 s and up to 30 s (Iggo, 1960), (Iggo and Kornhuber, 1968). The precise time of cessation of stimulation is likewise obscured by their prolonged after discharge (Burgess and Perl, 1973).

These C fiber receptors have elevated thresholds (25 mg to 7.5 g) as compared to myelined velocity detectors and their rate of firing is slower: less than 100 impulses/s as compared to a peak of 100 impulses/s in the myelinated receptors just described (Iggo, 1960). The conduction velocity of their primary afferent C fibers is of course much slower than the myelinated primary afferents (.55-1.25 m/s) (Iggo, 1960). The receptive fields of each C fiber are small, 2-5 mm sq., so they probably give rise to a fairly well-localized, lingering sensation when stimulated by a slow-moving stimulus.

The velocity detectors innervated by C fibers fatique rapidly. When stimulated at intervals of less than 3 minutes, the response decreases in amplitude and increases in latency (Iggo and Kornhuber, 1968). At intervals of less than 1 min, the minimal time of contact of the stimulus within the cutaneous field of the neuron exceeds 500 ms (Burgess and Perl, 1973). This fatigue appears to originate in the receptor and not in the axon.

Whitehorn, Howe, Lessler and Burgess (1974) determined the percentage of myelinated fibers that each of these position and velocity detectors contribute to the accessory sural nerve of the cat, together with the area of cutaneous fields of some of the receptors:

TABLE II

Receptor	Percent	Fields, cm^2
Type I	6.7	
Type II	4.4	
G 1 Hair	4.6	2.2-2.7
Intermediate Hair	3.0	1.4-2.3
G 2 Hair	10.2	0.7-0.9
Down Hair	28.9	0.4-0.5
F 1 Field	3.3	2.0-2.5
F 2 Field	17.6	2.0-2.9

Together the myelinated fibers make up about 25% of the fibers in cutaneous sensory nerve, the other 75% of fibers are unmyelinated C fibers most of which are probably nocireceptors, while some, like those discussed, are receptors of non-noxious mechanical stimuli.

The third group of receptors in hairy skin are those specialized for detecting rapid transients. Two will be discussed here, the Pacinian corpuscle and the G 1 hair receptor.

Pacinian corpuscles are found in hairy skin and are also plentiful in glabrous skin, external genitalia, mammary gland, in the deep dermis associated with blood vessels, along nerve trunks, fascial planes, in joint capsules, pleura, even in the pancreas and lymph nodes (Sinclair, 1967). Most physiological studies are done on Pacinian corpuscles from the mesentery of cats, where they are easy to dissect out with their primary afferent axon.

Pacinian corpuscles are 1-4 mm long and 0.5-1.0 mm in diameter and are elliptical in cross-section (Hubbard,

1958), (Sinclair, 1967). The Pacinian corpuscle has an inner core containing the nerve fiber, inner lamellae, and albuminous fluid with cholinesterase activity. Outside of the central core is a space filled with fluid, collagenous fibers, blood vessels and some free cells. Surrounding this layer is a cellular growth zone whose cytoplasmic extensions across the fluid-filled space to form the bulk of the inner core (Pease and Quilliam, 1957). Surmounting this growth zone are the most conspicuous element of the corpuscle, the outer layer of 20 concentric lamellae which are continuous with the perineural sheath (Shanthaveerappa and Bourne, 1963). Each lamellae is formed by a flattened cell less than one micron thick (Sinclair, 1967). Together the non-nervous elements make up 99% of the bulk of the organ (Sinclair, 1967).

Unlike the outer lamellae, the lamellae of the inner core are not concentrically arranged with radial symmetry, but consist of two bilaterally symmetrical cylindrical halves on either side of the axon separated by a cleft above and below. Fig #5. The lamellae of the inner core are of about the same thickness as those of the outer core but are more closely-spaced together. The perikarya of the core lamellae lie in or near the intermediate growth zone, and send cytoplasmic arms into these superior and inferior clefts. The arms then branch and terminate as lamellæ which interdigitate with those of the cytoplasmic extensions of

cells from the opposite side of the corpuscle (Pease and Quilliam, 1957). A node of Ranvier is always found just proximal to the point of entry of the terminal nerve fiber into the corpuscle (mean distance 55 micra, range 0-150 micra), while the diameter of the fiber at that segment is 4.5-6.9 micra. The nerve fiber follows a tortuous course in the proximal part of the corpuscle stalk. Another node of Ranvier is seen halfway along the length of the fiber in the stalk (Quilliam and Sato, 1955). On entering the central core the fiber becomes narrower, straight, and elliptical in cross-section. It loses its Schwann cell sheath, which is not continuous with the core lamellae (Pease and Quilliam, 1957) and ends near the distal extremity of the corpuscle frequently by bifurcation. Each branch ends in a terminal swelling 8-12 micra in diameter (Quilliam and Sato, 1955).

The Pacinian corpuscle reacts to vibration, a repeated rapid mechanical transient, deforming it as little as 1 micron at frequencies of 150-400 Hz, but is not discharged by larger amplitude displacements at frequencies less than 40-60 Hz (Burgess and Perl, 1973). Pacinian corpuscles stripped of their outer lamellae do not display this selectivity of response, suggesting that the outer lamellae of the corpuscle act as a sort of mechanical fiber, allowing only high velocity mechanical stimuli to excite the axon of the inner core (Hubbard, 1958).

Hubbard studied the reaction of Pacinian corpuscles isolated from the mesentery of the cat to deformation of up to 20 microns at velocities of 2.5-40 micra/s by means of flash photography. Measurement of the lamellae before deformation showed that the spacing of the layers is logarithmic, i.e. the radii of successive lamellae with respect to the long axis of the corpuscle could be defined by the successive terms of a geometric series.

Stimulation of the corpuscle by deformation of even 40 times threshold and 2.5 times critical velocity failed to bend or change the length of the axon within the inner core, showing that mechanical displacement of the axon itself was not necessary for impulse generation. Hubbard found that for equivalent amounts of displacement of the outer lamellae, only deforming stimuli of very high velocity caused the wave of deformation to be transmitted through all the lamellae to the inner core. He hypothesizes that the enclosed fluid between the outer, widely-spaced lamellae are able to absorb the force of a slow deformation but offer resistance to and transmit the impact of a deformation at high velocity, just as a door on a hydraulic damper can be opened easily if opened slowly but offers great resistance to a quick shove.

Mechanical stimuli to the Pacinian corpuscle cause a discharge in the axon terminal called the generator potential. When the generator potential exceeds a critical magnitude

it serves to initiate the all-or-none propagated potential which travels to the CNS.

Hubbard proposes a mechanism by which deformations reaching the inner core might initiate a generator potential in the unmyelinated terminal. The mechanism hinges on the axon's shape-it is elliptical in cross-section and lies with its major axis along the cleft of the semicircular cytoplasmic plates of the inner lamellae. Hubbard hypothesizes that the production of the potential occurs along this elliptical unmyelinated section of the axon when mechanical stimuli cause transient changes in its membrane permeability. The major axis of the axon is only 3 micra and its minor axis is 2 micra. For an ellipse with this axis ratio of 1.5:1, the fractional change in perimeter is nearly 1/3 of any fractional change of the minor axis. A small decrease in diameter of the minor axis gives rise to a large increase in perimeter which can only occur if the molecules of the axon cell membrane become more widely-spaced leading to a greater leakyness of the membrane. Small changes in the diameter of a circle give almost no change in perimeter so that none of these proposed changes would occur if the axon was circular instead of elliptical in cross-section.

The Pacinian corpuscle is distinguished by a lack of linear directionality and an extremely short recovery cycle. No decrease in excitability to appropriate stimuli

is noted 5-6 ms after a propagated potential. Pacinian corpuscles accommodate rapidly. Only 2 or 3 propagated potentials are produced by each stimulation. The generator potential remains measurably elevated but only a few impulses are initiated in the axon. The Pacinian corpuscle is apparently "designed" to respond to repeated stimuli at short intervals (Burgess and Perl, 1973).

The second receptor in hairy skin specialized to signal rapid mechanical transients is the G 1 hair receptor, mentioned in the discussion of receptors on guard hairs. The G 1 receptor responds to movements greater than 50 micra of stiff hair shafts at guard hairs. Like the Pacinian corpuscles, the G 1 hair receptor fails to respond to even large amplitude sinusoidal stimuli at frequencies less than 60-80 Hz. The amplitude of a stimulus threshold decreases as frequency increases from 80-200 Hz. Unlike the Pacinian corpuscle which can respond to distant vibrations, the G 1 hair receptor responds only to stimuli which directly displace the hair shaft that it innervates. The G 1 hair receptor displays little linear directionality, has a short recovery cycle with no depression in excitability 10 ms after stimulation, and like the Pacinian corpuscle, shows rapid accomodation producing only 2-3 propagated potentials with each stimulus (Burgess and Perl, 1973).

Mechanoreceptors in Glabrous Skin

The mechanoreceptors in glabrous skin have not been

studied as extensively as those in hairy skin. Many of the same receptors are found in both locations such as Type I, Type II, F 1, F 2, and Pacinian corpuscle (Burgess and Perl, 1973). In addition, Meissner corpuscles in the dermal rete pegs of glabrous skin give rise to a discharge similar to that of F 1 and F 2 receptors. Meissner corpuscles were studied by Krause (1881) in post-mortem specimens of skin from the volar surface of the human finger.

Unlike the other corpuscles discussed, several Meissner corpuscles share one myelinated primary afferent nerve (Sinclair, 1967). Each myelinated branch ends in 2-9 myelinated terminal branches which enter the base and sides of the corpuscle (Cauna and Ross, 1960). In electron micrographs of biopsied corpuscles the axons are observed to lose their Schwann cell sheaths and meander between flattened irregularly-spaced cellular lamellae. The lamellar cells are continuous with the perineurium of the axon. The membranes of a lamellar cell become slightly thickened at places where it is closely apposed to the axolemma and many small vesicles are found in the cytoplasm of the lamellar cell membrane at these appositions suggesting a synapse (Cauna and Ross, 1960).

Mechanoreceptors Associated with Sinus Hairs

Sinus hairs or tylotrichs are the largest and thickest hairs on the bodies of mammals. In the cat they are found on the forelimb where they are called carpal hairs and on

the nose or mouth where they are the familiar whiskers or vibrissae. Blinded cats without vibrissae have difficulty walking through a narrow passage while blinded cats with vibrissae do not (Nilsson, 1969). Carpal hairs are most common in animals like the raccoon that use their forelimbs to grasp and feel their food (Nilsson, 1969).

The structure of the tylotrich or sinus hair is complex. There is an external sinus wall, a layer of strong connective tissue, an internal sinus wall, a glassy membrane, and finally, the external root sheath surrounding the hair itself (Nilsson, 1969). Between the external and internal sinus walls there is a connective tissue-filled space surrounding a ring sinus filled with blood from which the hair gets its name.

Between the glassy membrane and the external root sheath are a collection of large Merkel cells with clear cytoplasm (Nilsson, 1969), like those in the Type I receptor dome. The connective tissue of the inner hair follicle is also supplied with straight and branched lanceolated terminals of myelinated nerves (Andres, 1966). Each tylotrich is innervated by multiple fiber filaments of its own myelinated primary afferent axon, each filament ending in a lanceolated terminal (Nilsson, 1969).

The Merkel cell tylotrich receptors signal both position and velocity changes with a slowly-adapting discharge similar to that of the Type II receptor in hairy skin. With

increasing velocity of displacement, the afferent discharge frequency increases as a power function with an exponent between 0.3 and 1.1.

The velocity-detecting response of the tylotrich receptor unit occurs only with movement away from the resting position but the position-detecting function behaves quite differently. In contrast to guard and down hairs which exhibit maximal activity during extreme displacement in one preferred direction, an intermediate response at the intermediate position, and minimal activity at the opposite extreme, the sinus hair receptor shows a graded discharge as it is displaced from the rest position in any direction. Since the sinus hair is surrounded by Merkel cells, displacements in any direction lead to progressively increased activity in a different population of Merkel receptor cells innervated by different fibers of the multi-fiber filament. The receptors then probably signal the specific direction of displacement of the sinus hairs.

The second group of receptors associated with sinus hairs are Pacinian corpuscles which have been described. As in other tissues they detect rapid mechanical transients and respond without linear directionality. They are notably absent from vibrissae but are plentiful near carpal hairs (Burgess and Perl, 1973).

Local Electrical Anesthesia

Efforts to produce analgesia and anesthesia by passing

electric currents through the skin date back to the ancient Greeks who made use of the currents produced by the electrical fishes (Torpedo mamoratus, Malapterurus electricus and Gymnotus electricus) to ease the pains of gout.

Galen employed the live torpedo fish as an anodyne in various illnesses, including headache (Kane, 1975). In the 17th century Redi, Perrault, Richer, Borrelli, and Lorenzini noted the numbness produced by the torpedo fish (Kane, 1975). Cavendish and Walsh reproduced with a modified Leyden jar the same paresthesias and numbing sensations that they felt on touching the live torpedo fish (Kane, 1975).

Dentists were pioneers in the modern use of electric currents against pain. An American, W.G. Oliver in 1857 attached the negative pole of a battery to a pair of tooth extracting forceps and had the patient hold the positive pole. The tooth was extracted while being electrified through the forceps by a current that was not well-characterized, but which was possibly of high frequency. Patients reported varying decreases in pain during the extractions (Kane, 1975).

The first modern medical application of a well-characterized electrical current (A.C., 2000 Hz) was in 1933, by Dr. Percy Turnure at the Vanderbilt clinic, who used it as the sole anesthesia to lance a painful felon in the forefinger of a young woman (Thompson, Banks, Barron, Fratio, and Mattison, 1934). The effect was further

characterized by Thompson et al. (1934) who found that currents between 50 and 250 Hz produced the greatest elevations of sensory threshold and that the sense of pressure, was most sensitive to the effect, followed by touch, and pain in descending order, with little consistent change in the detection of heat and cold.

Local electrical anesthesia has been used with varying success to treat chronic pain syndromes. Meyer and Fields (1972) reported an immediate, reproducible relief of pain in unbiased patients with "causalgia" during stimulation proximal to the site of injury with .1 ms square wave pulses at 100 Hz. They reported that for the effect to occur, non-painful paresthesias had to be appreciated by the patient in the area of distribution of the stimulated nerve.

Campbell and Taub (1973) stimulated the index and middle fingers of human subjects via surface electrodes with 1 ms bursts of 100 Hz direct current at 1-5 mamps and at 10-12, 22 and 50 volts. They found that the threshold to light touch over the stimulated area was raised in direct proportion to the voltage applied and that at voltages exceeding 22, thresholds for painful stimuli were also proportionately raised.

Campbell and Taub (1973) then compared the effects of similar stimulation (100 Hz DC at 50 v, and 1-5 amps) when it was delivered first in 0.5 s bursts every 30 s for 20 minutes

and then continuously for the same time. The amplitudes of the median nerve action potentials were recorded via signal averaging apparatus from surface electrodes at the wrist of the stimulated hand. Subjects receiving bursts of stimulation reported painful paresthesias each time the current was applied. The median nerve action potentials recorded with latencies corresponding to velocities of 293 ms and 16-23 ms were interpreted respectively as the A-alpha and A-delta components of the afferent volley.

On continuous stimulation with the same electrical parameters obtaining, subjects reported strong paresthesias which were painful only for the first minutes. After a short time the pain disappeared and the paresthesias felt were less intense. The first peak in the median nerve action potential was increased in latency and decreased in amplitude during continuous compared to intermittant stimulation. The second peak, designated A-delta, was either greatly diminished in amplitude or failed to appear altogether during continuous stimulation. Campbell and Taub interpreted their results in the light of experiments by Collins et al (1963), described above, in which A-alpha fibers were found to transmit tactile and A-delta fibers to transmit painful sensations. Fatigue of the A-alpha fibers on continuous stimulation was thought to be reflected in the increased latency and decreased amplitude of the first peak and in the decreased intensity of the paresthesias perceived by the subjects. Increases in the threshold to light touch

in the first experiment were thought to be due to impaired conduction of the A-alpha afferent volley. Similarly, the elevation of the threshold for pain in the first experiment and the gradual disappearance of painful sensations on prolonged continuous stimulation in the second were thought to be caused by peripheral blockage of the A-delta potential.

Hoffert (1974) used an experimental set-up for stimulating and recording from the median nerve which was very similar to that of Campbell and Taub (1973). He applied a continuous 0.5 ms, 100 Hz, 50 v, 3-6 mamp direct current to the 1st phalanx of the middle finger. The stimulus was applied to the third phalanx of either the middle finger or the index finger of the same hand and consisted of 0.1 ms D.C. pulses at 1 s intervals (voltage and amperage were the same as the proximal current). Hoffert found that when the continuous and intermittant currents were applied to the same finger, the subjects perceived the intermittant current as less painful and the median nerve action potential recording for the intermittant current was smaller in amplitude than when the intermittant current was applied alone. In contrast to this, when the continuous and intermittant stimulating electrodes were on separate fingers, the subjects reported no subjective decrease in pain during intermittant stimulation and the recorded median nerve action potentials recorded from intermittant stimulation were not decreased by the continuous stimulation.

The median nerve action potential recorded by Hoffert consisted of a sharp peak very similar in contour and latency to the A-alpha peak of Campbell and Taub (1973). However, at no time was Hoffert able to detect the peak designated by Campbell and Taub as the A-delta potential. This negative finding was corroborated by the later work of Kane (1975) and in our work, both using an experimental set-up very similar to that of Campbell and Taub (1973).

The experiments described in this paper were designed to characterize further the effect of electrical anesthesia: the relationship between the depth of anesthesia and the amplitude of the median nerve action potential at the wrist, possible spread of the effect to unstimulated areas, the existence of an anesthesia at subliminal levels of electrical stimulation, and the time course of the anesthesia were studied. For an extensive review of the history of electrical anesthesia see Kane (1975).

THE EXPERIMENTS

Experiment I

Campbell (1973), Hoffert (1974), and Kane (1975) showed in their experiments that the increased thresholds to mechanical and painful stimuli on stimulation with 100 Hz direct current was accompanied by a decrease in the ability of the stimulated nerve to be discharged by electrical stimuli. This effect was documented by recording the median nerve action potential at the wrist and correlating its decreased amplitude with elevation of sensory thresholds.

In this experiment, we attempted to stimulate the digital nerves at voltages high enough to produce elevated thresholds to touch, but not high enough to produce decreases in the amplitude of the median nerve potentials. It was our hypothesis that electrical anesthesia is not dependent for its effect on block of primary afferent impulses to the CNS and that the two effects are unrelated and can be dissociated.

Method

Seven unpaid subjects (5 males and 2 females) between the ages of 22 and 25 participated in the experiment. They were not instructed on the purpose of the experiments or the expected effects of the electrical currents on sensory thresholds. The function of the stimulating and recording electrodes, however, was explained to them.

The experiments were conducted in a small quiet room reserved for the purpose. Only the experimenter and the subject were present during the runs. There were no interruptions or spectators to distract the subjects.

The hair was removed from the skin on the middle finger of one hand and from the volar surface of the forearm near the wrist by means of a depilitory agent (Surgex or Nair). The skin was then washed with acetone and with water to remove the layer of dead epidermal cells and improve electrode contact.

Next one disposable adhesive EKG monitoring electrode was placed over the median nerve on the volar surface of the wrist centered between the palmeris longus and flexor radialis tendons just proximal to the carpal tunnel. The second electrode was placed just proximal to the first on the volar surface of the forearm. A dab of Cambridge electrode jelly was added to the jelled electrode contact. The electrodes were further secured by taping them with paper intravenous tape. Impedence was then measured with a Grass Impedence meter. Satisfactory recordings were obtained when an impedence less than 40 KOhms and preferably less than 20 KOhms was recorded.

Disa, saline-soaked, felt-covered finger electrodes were placed on the middle finger of the same hand to which the recording electrodes were attached. The cathode and the anode were placed around the proximal and distal interphalangeal

joints respectively. A thin layer of petroleum jelly was spread between the electrodes to prevent them from short-circuiting across the skin. These electrodes were kept moist by wetting them with saline delivered through a Pasteur pipette at 10 min. intervals or between each recording. Impedences across the Disa electrodes was then measured. A value greater than 30 KOhms usually signified that no short-circuiting had taken place across the electrodes.

A large felt-covered grounding electrode was secured around the stimulated hand at the palm and was kept moist with saline.

A Devices Gated-Pulse Generator driven by a Devices Digitimer stimulated the subject through the finger electrodes. The Gated-Pulse Generator delivered .1 ms pulses at 30 volts and was triggered by the Digitimer at 1000 ms or 10 ms intervals (frequencies of 1 and 100 Hz).

The recording electrodes and the ground were connected to a Grass amplifier set at 100,000 times amplification. The low filter was set at 1 HKz and the high filter at 30 kHz. One hundred and twenty eight action potentials were stored and signal-averaged by a Nicolet model 1074 computer and recorded visually on a Nicolet slave oscilloscope. The computer was activated 5 ms before the test stimulus so that the stimulus artifact always appeared 5 ms into the oscilloscope trace and could then be used to time the peak of the

recorded action potential.

The time and amplitude of each signal-averaged median nerve action potential was measured by means of a courser light on the Nicolet slave oscilloscope whose position could be converted to a digital read-out on the oscilloscope by the computer. A photograph was then made of the recording with a Polaroid camera. Fig #7.

After the electrodes were attached to the subject, sensitivity to light touch was measured by means of a Cochet and Bonnet Esthesiometer which is a calibrated Von Frey hair. The Esthesiometer employs a thin nylon filament with a diameter of 0.12 mm. The force required to bend the filament when a vertical tap is delivered to the skin is inversely related to the length of the filament (Table III). The hair is calibrated so that the length of the filament in mm can be related to a blow of known force in grams/sq. mm. In this experiment, the threshold to light touch was not actually measured since all subjects could feel the lightest touch that the Esthesiometer could deliver. The instrument was very useful, however, in measuring changes in sensitivity to light touch.

Touch testing in this experiment was done by having the subject close his eyes and say "yes" when he thought he had been touched. A brisk vertical tap was delivered so as to make contact with the skin but not to stroke it with the filament. The volar surfaces of all the phalanges were

touched during testing, but only the thresholds of the first and third phalanx of the stimulated finger was recorded. After three consecutive negative response (three touches to which there was no response), interrupted by testing on other fingers, the strength of the stimulus was increased by a step on the Esthesiometer's graded scale, and the procedure repeated until a stimulus strength was reached at which the subject gave three positive responses separated by testing on other fingers of the same hand.

After the subject was tested with the Esthesiometer, the Digitimer and pulse generator were set to deliver a 30 v, 1 Hz stimulus with a pulse width of .1 ms and 128 propagated potentials were recorded, amplified, and signal-averaged as described. Touch thresholds were again measured. The amplitude of the recorded afferent volley was measured at its maximum height using the oscilloscope courser and digital read-out. The distance of the peak from the stimulus artifact was also noted. Since the stimulus artifact always appeared 0.5 ms into the oscilloscope sweep, it was possible with this known time to distance ratio to calculate the latency of the median nerve action potential. A photograph was then made of the recording on the oscilloscope.

Now the voltage knob was turned to zero and the instruments were reset to deliver the same stimulus but at 100 Hz. The subjects were asked to gradually increase the voltage up to 30 v. All subjects accomplished this in less

than 10 min. As soon as 30 v was attained, another recording was made of 128 propagated potentials and threshold to light touch was tested. Voltage was then maintained at 30 and recordings and tests of thresholds done as described at times 3, 5, 10, 15, 20, and 25 minutes. After 25 min., the stimulation was stopped and measurements were taken at 30 min. The impedence at the recording and stimulating electrodes were measured again.

Results

All subjects were able to feel the lightest touch of the Esthesiometer, .96 g/sq. mm on all fingers both before stimulation and when they were being stimulated with 30 v, .1 ms pulses at 1 Hz. (Table IV, V).

Upon stimulation with the 1 Hz currents subjects reported a strong throbbing sometimes painful tapping sensation extending from the stimulating electrodes to the tip of the stimulated finger.

Stimulation at 100 Hz resulted in a biphasic sensation. At the onset of stimulation and with each increment in voltage, there was a sharply painful prickling or buzzing paresthesia which lasted about 15 s. This was succeeded by a bright pins and needles or buzzing sensation which was not painful, but which was described by some subjects as "nerve-racking".

The threshold to light touch at the terminal phalanx was increased in all subjects on stimulation with currents

at 100 Hz as soon as a voltage of 30 v was reached, time 0, and showed no consistant changes in threshold at all times tested. In subjects 3, 4, 6, and 7, the threshold to light touch was at or lay above the maximal stimulation that the Esthiometer could deliver, 17.68 g/sq. mm at all times that it was measured. In subjects 1 and 2, thresholds varied during the experiment, without apparent pattern 17.68 g/sq. mm and 12.84 g/sq. mm, the penultimate reading on the Esthiometer.

In all subjects except number 4, who required 10 min., the sensitivity to touch on the distal phalanx had returned to control levels 5 min. after the stimulation was stopped.

The linear arrangement of the electrodes gave rise to a biphasic wave representing the summation of the afferent volley as it passed the electrodes. Since it was recorded with surface electrodes, its amplitude varied from subject to subject depending on the amount of intervening tissue present and on the exact position of the surface electrodes with respect to the course of the median nerve in the subject. Therefore, absolute comparisons of the amplitude of the median nerve afferent volley were not possible with this technique. Instead, the response at 1 Hz is taken as a baseline for each subject, since the nerve will not fatigue when stimulated only once each second. Subsequent recordings at 100 Hz were calculated as percents of the amplitude of the baseline recording at 1 Hz (Table IV).

All subjects showed some decrease in the amplitude of the afferent volley on stimulation of the digital branches of the median nerve at 100 Hz. The mean decrease was 21.7% (range 3-58.7%). In all subjects but one, this decrease occurred within the first 10 min. of stimulation at 100 Hz. The mean time of maximal decrease in amplitude was 6.8 min.

All subjects but the first showed increases in the latency of the median nerve action potential measured at the wrist during 100 Hz stimulation for 25 min. (Table VI). The mean increase was 0.25 ms, the minimum increase was 0.06 ms, the maximum increase was 0.71 ms.

In 3 of the 7 subjects there was an increase in amplitude of the median nerve afferent volley in one or more of the recordings. The maximum increases in each of the 3 subjects were, 42.7%, 36.7%, and 41.3% (mean 40.1%, at 5, 25, and 10 min. respectively).

Experiment II

In previous experiments with electrical anesthesia, elevations of sensory thresholds have always been associated with the sensation in the subjects of prickling paresthesias. In this experiment we investigated the possibility of electrical anesthesia at voltages that produced stimulation below the electrical sensory threshold.

Five subjects, all males ages 21-30, participated in this experiment. One subject had participated in experiment I, the other four had no experience with the experiments before.

The subjects were told nothing about the intent of the experiments or what kind of sensations to expect from electrical stimulation.

Subjects were prepared and electrodes placed as in Experiment I. Control thresholds were tested as before, this time on the volar surfaces of all 3 phalanges of the stimulated finger, i.e. proximal to the stimulating electrodes, between the electrodes, and distal to the electrodes.

The stimulus was then set at 100 Hz, .1 ms, and the subjects were asked to gradually turn the voltage knob up without looking at it, to the point where they just became aware of a different sensation in the stimulated finger, and then to slowly turn down the voltage until the sensation disappeared. The voltage was then turned to 0 and the procedure was repeated twice more. The mean threshold and the mean maximal imperceptible voltage were then calculated.

The voltage was set at the mean maximal imperceptible voltage for each subject and a baseline recording was made of 512 stimulus pulses at .1 ms and 1 Hz. Thresholds at the 3 phalanges were tested with the Esthesiometer.

The frequency of the stimulus was then changed to 100 Hz while the voltage remained at the maximal imperceptible voltage. Recordings of the afferent volley and measurement of thresholds were made at times 0, 5, 10, and 15 minutes. After the 15 min. measurement was taken, the voltage was increased to 15 or 20 v and 512 pulses were recorded to

verify that the stimulating and recording electrodes were operating correctly.

Results

All 5 subjects were able to feel the weakest stimulus of the Esthesiometer (.96 g/sq. mm) both before and during stimulation. Subliminal stimulation produced no measurable elevation of thresholds to light touch on either the 1st, 2nd, or 3rd phalanx.

Recordings made during subliminal stimulation showed a stimulus artifact but no measurable afferent volley peak. Recordings made at the end of the experiment at voltages of 15 or 20 v always showed a measurable peak.

Experiment III

Method

In this experiment we attempted to determine whether at any given voltage, the elevation of thresholds seen with 100 Hz, .1 ms direct current stimulation changes with time. We also measured how long it took for touch thresholds to return to control values after cessation of the stimulus. Voltages high enough to raise the touch threshold only moderately (1.40 or 1.84 g/sq. mm) were used, so that any fluctuations in sensory thresholds would be within the range measurable with the Esthesiometer.

A group of new subjects, 5 males and 3 females, 22-37 years old participated in this experiment. Only stimulating

electrodes were used. Thresholds were determined at the 2nd and 3rd phalanges of the stimulated finger as before. The subjects were then asked to turn the voltage up by steps just large enough to produce a change in sensation. At each increment in voltage, thresholds were measured at the 2nd and 3rd phalanges. When the threshold on the 3rd phalanx had increased to 1.40 g/sq. mm (1.84 in subject 3) the time (time 0) and voltage was noted. Thresholds at the 2nd and 3rd phalanges were then measured at this voltage at times 5, 10, 15, and 20 min.

After the final measurements current was turned off and the time, in seconds, for return of touch thresholds to control levels in the 2 phalanges were noted.

Results

The measured voltage required to increase the touch threshold at the 3rd phalanx to 1.40 g/sq. mm averaged 13.6 v (s=3.0 v). When the threshold was 1.40 g/sq. mm at the 3rd phalanx, the mean threshold at the 2nd phalanx was 1.81 g/sq. mm (s=.49 g/sq. mm) indicating that the skin between the electrodes is affected by the currents slightly more than the skin distally.

There were some fluctuations of sensory thresholds over time (Table VII), but these did not show a discernible pattern. In two subjects, no threshold measurements were made at time 0 for the 2nd phalanx (P2), but for the 6 subjects where this measurement was made, 5 showed an

increased threshold to light touch at some time compared to time 0 (maximum=.80 g/sq. mm, mean=.56 g/sq. mm), 2 showed both increases and decreases in thresholds at the 2nd phalanx. At the 3rd phalanx (P3), 7 subjects showed increases in thresholds to light touch (maximum=1.00, mean=.49 g/sq. mm) and 2 showed decreases (maximum= -.24, mean=.16 g/sq. mm). The 2 subjects showing decreases in thresholds, had increases in thresholds at other times in the experiment.

In summary, although there were some fluctuations in thresholds to touch, these fluctuations showed no evident temporal pattern, occurred in both directions, and were not of large magnitude.

Sensation returned extremely quickly after stimulation was stopped. In all 8 subjects sensation returned to control levels at the 2nd phalanx in 5 s or less. In all but one subject, threshold returned to control values in the 3rd phalanx in less than 15 s (mean=8s, S=5s). In the exceptional subject, threshold returned in 95 s. It appears that in most people recovery from low levels of electrical anesthesia occurs very quickly after stimulation is stopped.

DISCUSSION

Threshold Determinations

Before discussing the results of the experiments, some of the problems associated with sensory threshold testing in human subjects will be discussed. A human being or animal is equipped with various sensory detectors, e.g. for light, sound, chemical stimuli, and for detection of stimuli affecting the skin. The sensory detectors and their connections with the CNS must have a minimum energy of stimulation for each modality below which they fail to respond. In classical psychophysics, this is the threshold or limen. It is defined as a fixed level of signal strength or of a corresponding neural activity, below which no detection of the signal can occur, while above this level the signal is detected with certainty (Eijkman and Vendrik, 1963).

When thresholds are actually measured for a given sensory modality, there is never one stimulus strength above which the subject always correctly identifies the stimulus and below which he never detects it. Instead, for any stimulus strength over a wide range the subject gives a characteristic population of correct and incorrect responses which can be expressed as a graph in which frequency of correct responses is plotted against stimulus strength. In order to explain the existence of this curve and its shape, classical psychophysics assumes that either the signal varies

statistically, or that the threshold level varies or both (Eijkman and Vendrik, 1963).

Even more puzzling, is the observation that the subject will often perceive the stimulus when none was delivered. These mistakes are called false positives or false alarms. They are more frequent when the subject is told to expect the stimulus more often. They also occur more often in forced-choice experiments in which a stimulus is presented in one of "n" temporal intervals and the subject is asked to select the interval he believes to have contained the stimulus (Swets, Tanner, and Birdsall, 1971), (Mountcastle, 1974). Classical threshold theory has no explanation for false positives except to call them blind guesses, that is decisions not preceding from any specific sensory information.

A new model taken from statistical decision theory has been developed to explain why sensory thresholds cannot be measured absolutely. The new model also offers an explanation for false positives.

Instead of a stimulus, statistical decision theory introduces the concept of a "signal" that must be detected against a background of "noise" (Sinclair, 1967). The noise may be external distractions, such as input from other senses, or internal such as neural activity independent from that caused by the stimulus but present in the afferent fibers of the sensory receptor. The subject's task in detecting a stimulus is to decide whether a given interval

contains the noise plus the stimulus or the noise only. A model from game theory is helpful in explaining how this decision might be made (Swets, et al, 1961).

Suppose that someone is rolling three dice, two of which are ordinary dice while the third die has 3 blank faces and 3 faces with 3 dots on each face. You are not allowed to see the rolled dice, and you are asked to decide, from the total of the 3, whether the face showing on the 3rd die is 3 or 0. Inspection of Fig #7 shows that the way to maximize your correct answers is to decide on a cut-off point "c" along the x-axis of maximum overlap between the two curves such that when "x" is greater or equal to "c" you guess that the 3rd die face shows 3, and when "x" is less than "c", you guess that the 3rd die face shows a 0. The response criterion, "c" is not absolutely a function of probabilities, because if you are told that you will receive 5 dollars for identifying a throw with 3 showing on the 3rd die face, and that you will be fined 5 dollars for not identifying that event, your response criterion will move leftward toward lower values of "x". Similarly, different games can be devised in which the probabilities of two alternatives differ widely or in which the amount of overlap of the probability distributions varies.

In tests of sensory thresholds in people, the subject must decide whether a certain observation "x" is more likely to be a member of one or two partially overlapping probability

density curves. Fig #8. The first curve describes the probability that a certain sensory event of magnitude "x" will occur when noise alone is present $f_n(x)$. The second curve describes the probability of occurrance of the same sensory event when a signal is also present $f_{sn}(x)$. The subject is thought to make his decision, as in the dice game, by setting a response criterion or cut-off value $x=c$, such that for any "x" greater than or equal to "c", the observation is assigned the response "stimulus plus noise", and for any "x" less than "c", the observation is placed in the category "noise alone" (Mountcastle, 1974).

Just as in the dice game, the value of "c" is determined by the relative area of each probability curve, and by the amount of overlap of the two curves. The response criterion would also be sensitive to motivation, as in the dice game, and to expectation, as when a subject is told that a stimulus will be present in many test intervals. The signal detection model predicts that, for stimuli of low energies of any sensory modality, the incidence of false positives will be high.

Evidence that some kind of statistical decision system operates in the human brain comes from forced choice experiments. In the forced-choice experiments of Eijkman and Vendrik (1963), the subject was presented with 4 observation intervals. A stimulus consisting of deformation of the skin of the forearm of known magnitude was presented in 1 of the 4 intervals and the subject was asked to indicate in which

interval a stimulus was given. The subject had to also make a second choice different from the first.

Classical threshold theory states that the second choice will be a blind guess. But, according to the decision model, the subject must distinguish the stimulus from a background noise which is neural activity indistinguishable from the neural activity caused by small stimuli and which adds to the neural activity caused by stimuli. A correct first choice response will occur if the neural activity due to stimulus plus noise is larger than the neural noise in the other 3 intervals. A correct second choice response will occur if the neural activity due to stimulus plus noise in one interval is less than the neural noise in another and is greater than the neural noise in the remaining two intervals. By forcing the subject to make a second choice, it is possible to answer the key question of whether false positive responses are observations of noise indistinguishable from the signal, or mere guessing as threshold theory states. If the threshold model is valid, the second choice response can only be a guess. When the first choice is incorrect, the probability of a correct second choice will be 0.33, independent of the signal strength. The data of Eijkman and Vendrik (1963) shows, however, that when the first choice is wrong, the probability of a correct second choice is significantly higher than the threshold model predicts. In other words, the second choice contains a significant amount

of information about the stimulus.

The signal detection model is especially relevant to the experiments presented in this paper. The subjects were asked to identify a light touch delivered to an area of the skin in which they were feeling strong paresthesias. Experiments show that paresthesias do, in fact, arise within nerves, not in sensory receptors or in the CNS, and that they reach consciousness via the posterior columns (Merrington and Nathan, 1949). Paresthesias probably represent two kinds of noise. They are appreciated consciously, where besides being irritating and distracting, they flood the consciousness with "non-information" i.e. noise from the cutaneous area about which the subject is trying to make a sensory judgment. Paresthesias contribute to internal noise as well, which was defined earlier as neural activity indistinguishable from the neural activity caused by the stimulus.

One mechanism for the elevation of threshold to light touch seen in these experiments with high frequency electric currents is that paresthesias represent an additional form of noise leading to an increase in the response criterion and an elevation of "threshold". Experiment II shows that currents that are not sufficiently intense to produce paresthesias and are below the electrical sensory threshold do not produce elevations of the threshold to light touch. However, these low intensity currents also failed to produce a consistant median nerve action potential recording at the wrist. Failure to elevate light touch thresholds may have

been due to a lack of any significant afferent stimulation rather than to the lack of perceived paresthesias.

The second proposed mechanism for the effect of electrical anesthesia is that the electric currents cause a block in transmission of the nervous impulse at some point so that its perceived magnitude is decreased. The site of this block will be the subject of the second half of this discussion.

Receptor Potentials in Touch Receptors

In 1953 Gray and Sato, working with Pacinian corpuscles from cat mesentery, recorded neural activity along the segment of myelinated axon proximal to the first node of Ranvier. Following rapid mechanical stimulation of the receptor, the recording showed a triphasic response. The first phase was termed the receptor potential and was graded in amplitude with stimulus strength. The second was an ill-defined impulse thoughtto occur at the terminal axon of the Pacinian corpuscle. The third phase, or propagated potential, was an all-or-none response that was thought to originate in the first node of Ranvier, just before the axon loses its myelin sheath. The receptor and propagated potentials have been subsequently confirmed and characterized.

The receptor potential was found to increase with stimulus strength up to a maximum amplitude that never exceeds the amplitude of the propagated potential. If the axon was anesthetized with procaine and the propagated potential

abolished, the amplitude of the receptor potential could be made to exceed this maximum (Gray and Sato, 1953).

Loewenstein and Altamirano-Orrego (1958) were able to study the receptor potential and the propagated potential of the Pacinian corpuscle separately by taking advantage of the fact that the propagated potential has a longer refractory period than the receptor potential. They found that the receptor potential showed a graded increase in amplitude and rate of rise as a function of the strength of the mechanical stimuli, a constant latency, and spontaneous fluctuations in amplitude. Production of a receptor potential leaves the Pacinian corpuscle in a state of relative refractoriness which is probably caused by some change in the unmyelinated axon terminal. The amplitude of a second receptor potential produced during this relative refractory period is directly related to the time elapsed since the first response and inversely related to the amplitude of the first receptor potential. Receptor potentials are developed independently of the all-or-none propagated potentials and are not influenced by their refractory states.

Loewenstein and Mendelson (1965) hypothesized that the receptor potential in the Pacinian corpuscle was initiated in the unmyelinated axon terminal when stimulus energy was transmitted across the lamellae. The authors believe that the receptor potential upon reaching a critical level serves to initiate the propagated potential.

Ozeki and Sato (1965) found on direct measurement of the receptor potential that it attains its maximum amplitude at 1-2 ms and thereafter decays with an exponential time course and time constant of 1.2 ms. Encapsulated Pacinian corpuscles show no change in receptor potentials during maintained compression except during the transient states at the beginning and end of the compression. In constrast to intact Pacinian corpuscles, unencapsulated corpuscles respond to maintained compression with sustained receptor potentials similar to those seen in the slowly-adapting Type I and II mechanoreceptors.

Another cutaneous receptor in which a graded receptor potential initiates an all-or-none propagated potential is the tuberous organ (Knollenorgan), an electroreceptor of the lateral line system in the weakly electric mormyrid fishes, Gnathonemus petersii (Szabo, 1970) and G. stanleyanus (Roth and Szabo, 1972). Each tuberous organ consists of a group of 2-6 sensory cells each lying in a separate cavity in the epidermis. The surface of the cells are densely packed with microvilli. Just beneath the cell membrane is a multi-layered accumulation of mitochondria. All of the cells of a given tuberous organ synapse with the terminal branches of a single myelinated primary afferent axon. The tuberous organ is an example of an active sensory system. The electric field emitted by the receptor itself is distorted by objects in the environment and monitored by the receptor.

The receptor potential of the tuberous organ, recorded at the skin surface is thought to be a local phenomenon generated by the sensory cell membrane. It is distinguished from the propagated potential which is recorded from the afferent axon. Evidence is compiled by Roth and Szabo (1972) that the receptor potential is presynaptic with respect to the site of initiation of the propagated potential. First, the receptor potential may arise without initiating a propagated potential. Second, there is no delay between stimulation of the Knollenorgan and appearance of the receptor potential. Third, the time course of the receptor potential is not affected by cooling the tuberous organ (neural activity in which a neurotransmitter chemical must cross a synapse is slowed by cooling). Fourth, the receptor potential can be produced after the afferent nerve is transected and the fiber is allowed to degenerate.

The discovery of receptor potentials helped to explain an observation by Matthews (1931). He studied a muscle preparation from frog containing a single muscle spindle organ lying in the center of the muscle and responding to stretch. The frequency of the stretch-receptor response was proportional to the logarithm of the load. Matthews found that if he caused current of a few mamps to flow across the receptor, the frequency of the response rapidly declined. This effect did not occur if currents were directed centrally along the axon. Current research indicates that the effect

Matthews observed in the frog stretch-receptor may occur because currents directed into receptors block the generation of receptor potentials.

Lindbloom (1958) hypothesized that the inhibition of receptors by antidromic electrical currents occurs because receptors are constructed to respond to physiological stimuli in the same way. He studied mechanical receptors in the skin of the toad, Bufo bufo, by recording from the dorsal spinal root filaments, during mechanical stimulation of the skin. Each dorsal root filament innervates several receptors, whose morphology was not described, but which responded to vertical displacements of the skin of from 10-150 micra. Whenever one receptor of the unit responded to a mechanical stimulus above threshold, all of the receptors in the unit showed an absolute refractory period of from 3-6 ms and a characteristic increase in excitability over a period of 200 ms. Antidromic electrical stimulation of the afferent fiber at the dorsal root produced the same absolute refractory period and characteristic recovery cycle in all of the receptors of the unit. This finding suggests that mechanical stimulation in one receptor leads to impulses propagated antidromically to the other receptors in the unit resulting in a mutually inhibitory interaction.

Ozeki and Sato (1964) confirmed the hypothesis that block of receptor activity by antidromic electrical currents acts by inhibiting the production of receptor potentials and that

receptor potentials are necessary for the production of the propagated potential. Using the Pacinian corpuscles isolated from cat mesentery, they stimulated the afferent nerve fiber electrically and the corpuscle mechanically, and recorded both receptor and propagated potentials. Antidromic electrical stimulation raised the threshold of mechanical stimulation necessary to produce a receptor potential, until finally neither receptor nor propagated potential were produced. Ozeki and Sato further characterized the receptor potential noting that receptor currents produced by two successive stimuli delivered independently to two different sites on the unmyelinated terminal of the Pacinian corpuscle could summate to produce a propagated potential if the interval between the two stimuli was short.

Lindbloom and Tapper (1966) showed how the mutual inhibitory interaction discovered by Lindbloom (1958) operates during discharge of the multi-terminal tactile pad units in the hairy skin of cats. Discharge of one terminal in the unit, formed by the arborization of one primary afferent axon, causes the others to become refractory to stimulation. A time lag between stimulation of one terminal and inhibition in the others has been interpreted as an inter-terminal conduction delay. It is taken as evidence that mutual inhibitory interaction is effected by antidromic impulses conducted to all the terminal branches of the axon when the propagated potential from the stimulated receptor passes the point where the afferent axon arborizes. In this receptor, frequency of discharge is

proportional to the strength of the mechanical stimulus. Since inter-terminal conduction delay causes recovery to lag behind at sister terminals, a stronger stimulus, resulting in a higher frequency of discharge, is needed for a sister terminal to overtake the discharging terminal and to become the firing terminal. Unlike the Pacinian corpuscle in which subthreshold stimuli to different parts of the receptor create summating receptor potentials, no summation of receptor potentials occurs when different terminals of the same unit are simultaneously stimulated. Thus, in this multi-terminal tactile unit, the mutual inhibitory interaction insures that information is transmitted centrally from only one receptor terminal at a time. Perhaps the CNS of the cat is structured to read the information encoded in the frequency of discharge of single receptor terminals and could not decode the complex discharge patterns that would occur if more than one terminal caused discharge of the primary afferent axon.

If a receptor discharge has equal inter-spike intervals, then the mutual inhibitory interaction will result in a regular discharge pattern in the primary afferent axon. But how are irregular discharge patterns produced like that which occurs in the Type I mechanoreceptor on maintained mechanical stimulation?

The Type I mechanoreceptor is innervated by a myelinated fiber that arborizes within the epidermal dome. Each terminal arborization is capable of producing a receptor potential and of initiating a propagated potential. Irregular dis-

charge by the Type I mechanoreceptor could be produced one of two ways. Either many terminal branches discharge regularly at different frequencies and summate to produce an irregular pattern of propagated potentials, or one terminal branch discharges irregularly, inhibits the other terminals by antidromic block, and produces the irregular discharge in the afferent axon (Horch, Whitehorn, Burgess, 1974). Which mechanism is operating is not now known, but Horch et al. (1974) believe that the first is unlikely because it requires the Type I mechanoreceptor terminals to exhibit behavior different from that observed in other similar cutaneous receptors.

The Mechanism of Electrical Anesthesia

The three experiments described in this paper serve to further characterize the anesthesia produced by 100 Hz, .1 ms direct currents. There are 3 possible sites of action for the induction of this effect: 1. within the CNS 2. by conduction block in peripheral nerve and 3. at the cutaneous receptor.

Electric currents may produce anesthesia centrally by exciting a spinal cord inhibitory interneuron, perhaps in the substantia gelatinosa, which might block rostral transmission of sensory information. There is no indirect way of ruling out this possibility. The results of the experiments, however, suggest that a central mechanism is not responsible for the observed elevation of thresholds. If electrical

anesthesia were due to excitation of an inhibitory interneuron in the cord, some spread of effect outside the stimulated area would be expected because these interneurons typically have synapses at several spinal cord segments. But elevated thresholds were never seen on the stimulated finger proximal to the electrodes, or other fingers of the stimulated hand. These results are in agreement with those of Hoffert (1974). The effect was only seen in the skin between the electrodes and in the distal phalanx which is innervated by axons passing through the stimulated area.

Considerable attention has been given to the hypothesis that electrical anesthesia occurs by blocking conduction in peripheral nerve. Campbell and Taub (1973) and Hoffert (1974) found that during continuous high frequency electrical stimulations threshold elevations and the decrease in intensity of perceived sensations were associated with decreased amplitudes in the median nerve action potentials recorded. But, is electrical anesthesia caused by a blockade of transmission in the median nerve axons, or are these decreased median nerve action potentials only an associated finding? Kane and Taub (1974) stimulated the proximal phalanx of the index finger with continuous 50 v, 100 Hz .1 ms direct currents at an amperage 3 times the electrical sensory threshold. Subjects were then no longer able to feel the same current at 1 Hz delivered through electrodes on the distal phalanx of the same finger. The elevated electrical sensory threshold was

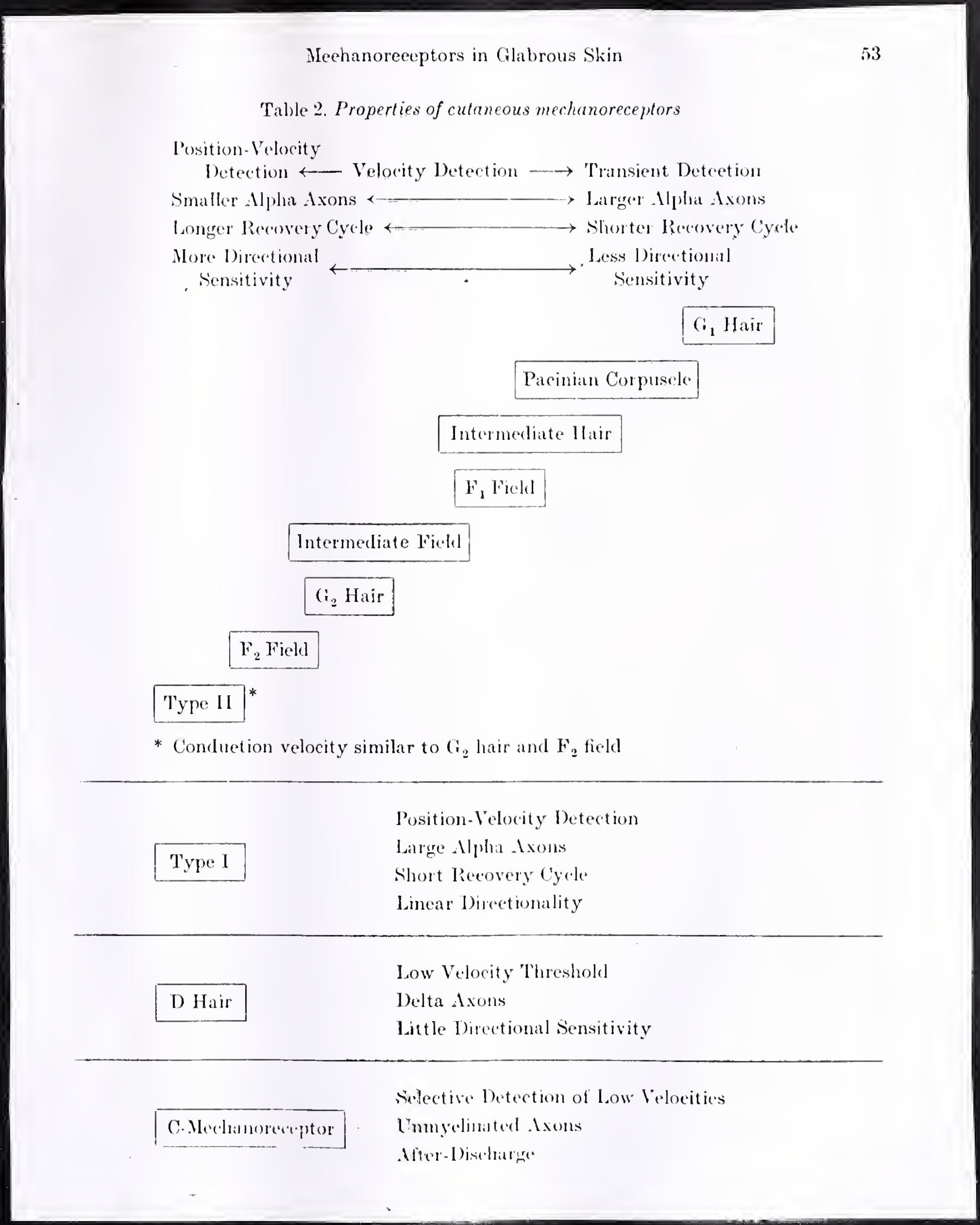
associated with a significant decrease in the amplitude of the digital nerve action potential measured through surface electrodes in the wrist. However, after 25 minutes of continuous stimulation, the propagated potential was seen to recover almost its original amplitude. Similarly in our experiment, early decreases in amplitude of the median nerve action potential were followed by recovery of 100% or more of amplitudes at 1 Hz, while in 2 of the subjects increases, rather than decreases occurred above amplitudes measured at 1 Hz. In conclusion, stimulation of the digital nerves at 100 Hz often produces signifigant decreases in the propagated potential of the nerve recorded at the wrist, but the inconstancy of this decrease, the presence of recovery, or of increases in amplitude with high frequency stimulation and the fact that all of these changes seem unrelated to the magnitude of threshold elevations indicate that peripheral nerve is probably not the mechanism of electrical anesthesia.

In experiments in which myelinated afferent nerves are repeatedly stimulated by electrical currents and then allowed to recover, a negative afterpotential is recorded, followed by a positive afterpotential (Gasser and Grundfest, 1936), (Schoepfle and Katholi, 1973). The negative afterpotential is of short duration and is associated with a relative hyperexcitability of the nerve (Gassner and Grundfest, 1936). The positive afterpotential is of much longer duration and is

associated with hypoexcitability of the nerve. The duration of decreased nerve excitability is often equal to the length of time the nerve is repeatedly stimulated. Gasser and Grundfest (1936) found that after 1 minute of "tetanization" of a mammalian A fiber, excitability was decreased for 1 minute. Schoepfle and Katholi (1973), found that after 20 s of stimulation of a frog myelinated nerve at 200 Hz the membrane of the nerve was hyperpolarized for from 20-30 s. The mechanism of electrical anesthesia might be post-tetanic hyperpolarization with decreased excitability (Kane, 1975). However, experiment 3 showed that thresholds to light touch return to normal very quickly after 20 minutes of stimulation, usually in less than 5 s. Post-tetanic hyperpolarization, with its slow time course, is probably not responsible for the elevated thresholds seen.

The third possible site of action for electrical anesthesia is at the receptor itself. The receptor acts as an energy transducer, turning a mechanical stimulus into a train of neural impulses in which information about the stimulus is encoded. In the receptors studied, a propagated potential is initiated by a receptor potential. The receptor potential is the indispensible link between the mechanical event of stimulation and the electrophysiological event of transmission. It is very sensitive to disruption by antidromic stimulation, occurs when one terminal of multiterminal mechanoreceptors begin firing under physiological

conditions. Experiments in which receptor potentials are measured directly show that the receptor potential is equally sensitive to disruption by antidromically directed electrical stimuli. Both kinds of antidromic inhibition show a recovery cycle on the order of ms. In our experiments, the elevation of thresholds to light touch on electrical stimulation was localized to the area between the electrodes and distally in skin innervated by axons passing through the stimulated area. The effect was characterized by very short recovery times. Although it is impossible to prove indirectly, a likely mechanism of action for these currents is by antidromic block of the receptor potentials and hence of the touch receptors within the skin.



Mechanoreceptors in Glabrous Skin 53

Table 2. *Properties of cutaneous mechanoreceptors*

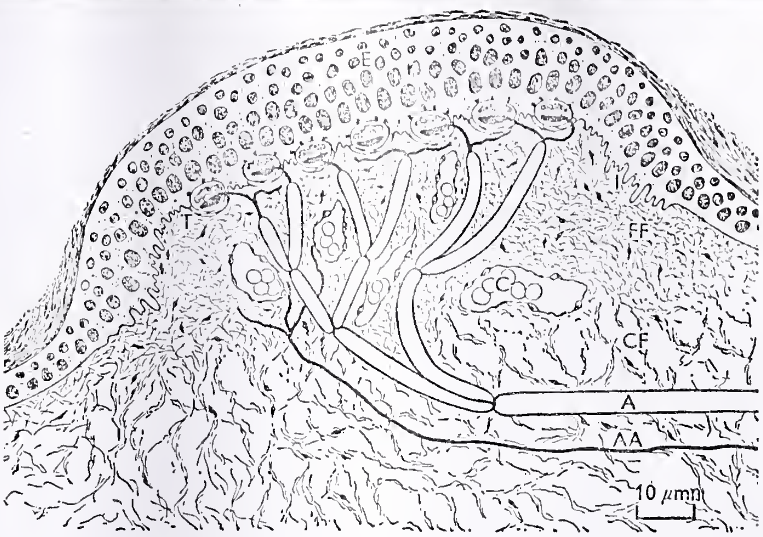
Position-Velocity Detection ← Velocity Detection → Transient Detection
Smaller Alpha Axons ←→ Larger Alpha Axons
Longer Recovery Cycle ←→ Shorter Recovery Cycle
More Directional Sensitivity ←→ Less Directional Sensitivity

G_1 Hair
Pacinian Corpuscle
Intermediate Hair
F_1 Field
Intermediate Field
G_2 Hair
F_2 Field
Type II*

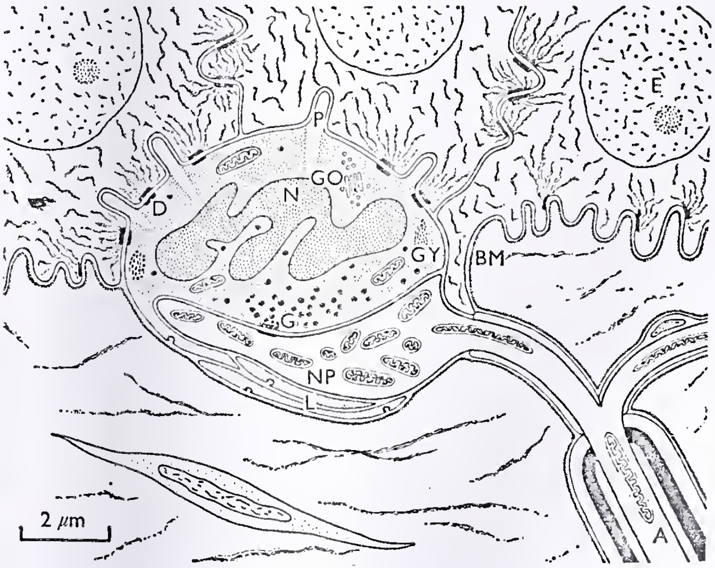
* Conduction velocity similar to G_2 hair and F_2 field

Type I	Position-Velocity Detection Large Alpha Axons Short Recovery Cycle Linear Directionality
D Hair	Low Velocity Threshold Delta Axons Little Directional Sensitivity
C-Mechanoreceptor	Selective Detection of Low Velocities Unmyelinated Axons After-Discharge

Figure 1 (from Burgess and Perl, 1973)



Text-fig. 1. A diagram showing the structure of a touch corpuscle as seen in light microscope sections. A, single myelinated axon; AA, non-myelinated axons; E, thickened epidermis of the touch corpuscle; FF and CF, fine and coarse bundles of collagen fibres; I, extensive indentations of the dermis by epidermis at the periphery of the corpuscle; T, tactile cell and its associated nerve plate; C, capillary.



Text-fig. 2. A diagram showing the structure of a tactile cell and its associated nerve plate. A, myelinated axon; BM, basement membrane; D, desmosome; E, epithelial cell nucleus; G, granular vesicles in the tactile cell near a junction with the nerve plate, NP; GO, Golgi apparatus; GY, glycogen; L, lamellae underlying the nerve plate; N, multilobulated nucleus; P, cytoplasmic process from the tactile cell.

Figure 2 (from Iggo, 1963)

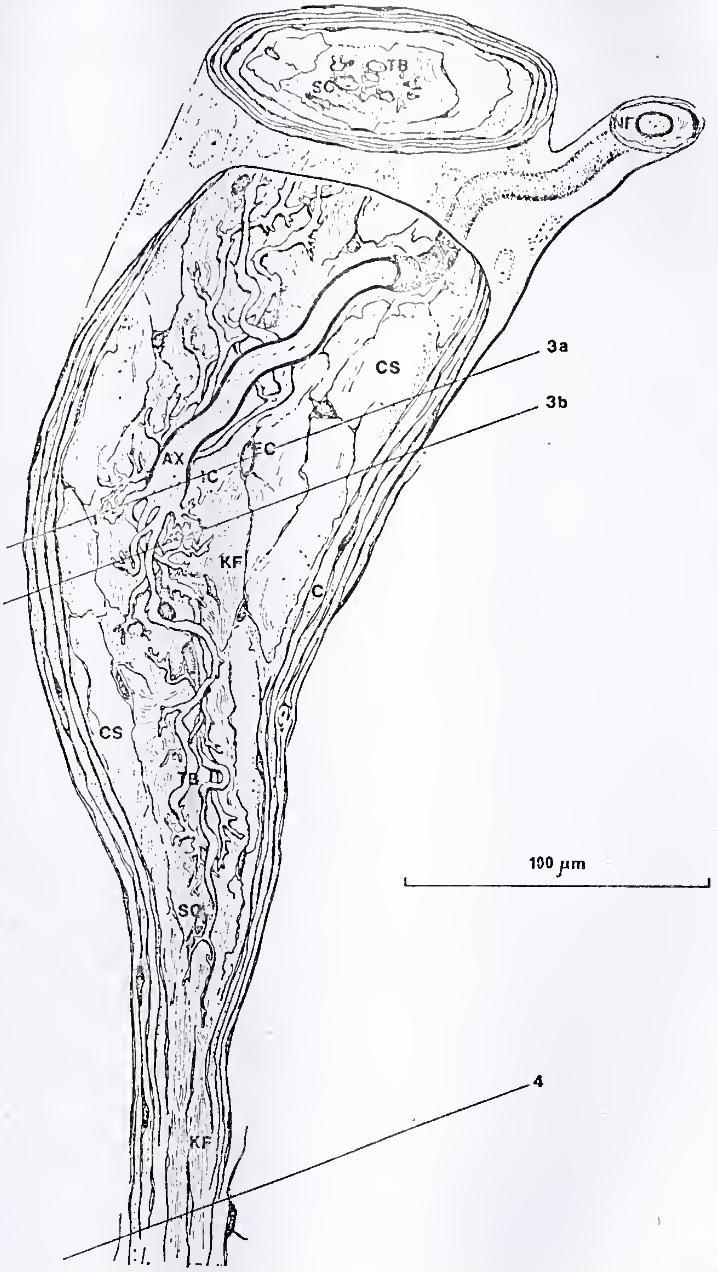


FIG. 8. Reconstruction of a Ruffini ending of the cat's skin from a series of semithin sections and from electron-microscope step cuts. The picture shows two-thirds of the 0·5 mm long Ruffini organ. Lettering as in Figs 5 to 7. Nerve fibre (nf). The drawn lines indicate the levels of Figs 3 and 4.

Figure 3 (from Andres, Duering and Iggo, 1972)

TABLE III. *Comparison of the properties of slowly adapting type I and II cutaneous mechanoreceptors.*

Similarities

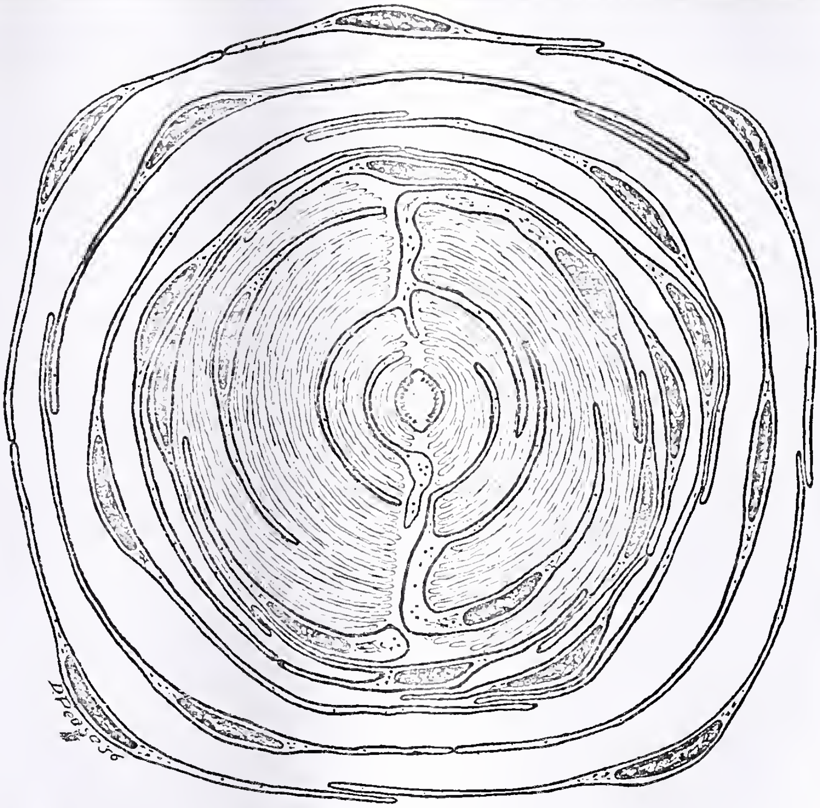
1. Slowly adapting. The discharge to maintained mechanical stimulus lasts for several minutes, at least.
2. Respond to vertical displacement of the skin—with dynamic and static components.
3. The dynamic response has both velocity and displacement components.
4. Found in cat, rabbit (Tapper, 1965; Brown and Iggo, 1967; Burgess *et al.*, 1968), the monkey (Iggo, 1963; Perl, 1968; Harrington and Merzenich, 1970) and units with similar properties in man (Boman and Hensel, 1960; Vallbo and Hagbarth, 1968; Knibestol and Vallbo, 1970).
5. Innervated by myelinated axons, conduction velocities ranging from 20 to 100 m/sec (mean 57 and 54 in cat, 47 and 31 in rabbit (Brown and Iggo, 1967)).

Differences

SA I	SA II
1. Irregular discharges to maintained stimulus	Regular discharge to maintained stimulus
Coefficient of variation $>0{\cdot}50$	Coefficient of variation $<0{\cdot}30$
2. Does not respond to stretching, unless severe and prolonged	Responds readily to stretching of the skin
3. Capable of high frequency discharge to all effective stimuli	Generally low frequency response to all effective stimuli*
Smallest ISI $<1{\cdot}0$ msec (>1000 Hz)	Smallest ISI 1·3 msecs (800 Hz)
4. Resting discharge unusual	Usually has a resting discharge
5. Distinct dome on surface of the skin (cat)	No evident surface feature
6. From 1–5 receptors per axon. These may be scattered over an area of 25 sq. cm.	One receptor per axon
7. Receptor terminals are Merkel discs associated with Merkel cells.	Receptor is Ruffini ending

* SA I units in the skin covering the dorsum of the hand in monkey (Iggo and Ogawa, unpublished) are more readily excited by stretching the skin than those described previously.

Figure 4 (from Burgess and Perl, 1973)



TEXT-FIG. 1. The central region of a Pacinian corpuscle is schematically presented in section to show the relations of cells of the intermediate growth zone to the lamellae of the inner core and also to the concentric lamellae of the peripheral zone. It is particularly important to appreciate that the core region is bilaterally organized. Connective tissue plates divide the closely stacked lamellae into two groups. The core lamellae are cytoplasmic continuations of cells whose perikarya are either in or at least close to the intermediate growth zone. Major cytoplasmic arms from these perikarya extend into the clefts of the core and from there branch laterally to form lamellae which interdigitate with those of other cells. In immature corpuscles there is no sharp transition between the lamellae of the peripheral zone and the intermediate growth zone. In adult corpuscles, however, there are but few cells left in the intermediate growth zone.

Figure 5 (from Pease and Quilliam, 1967)

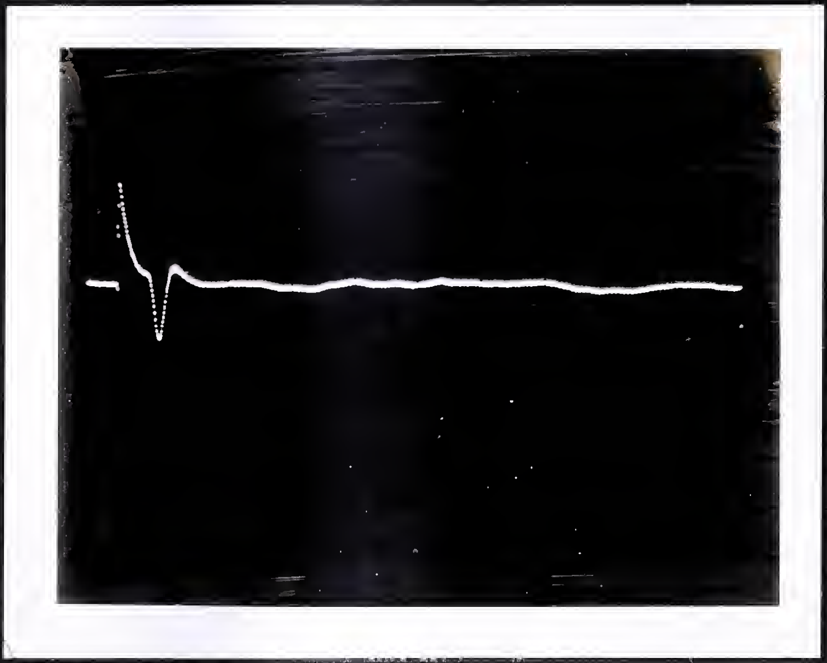


Figure 6

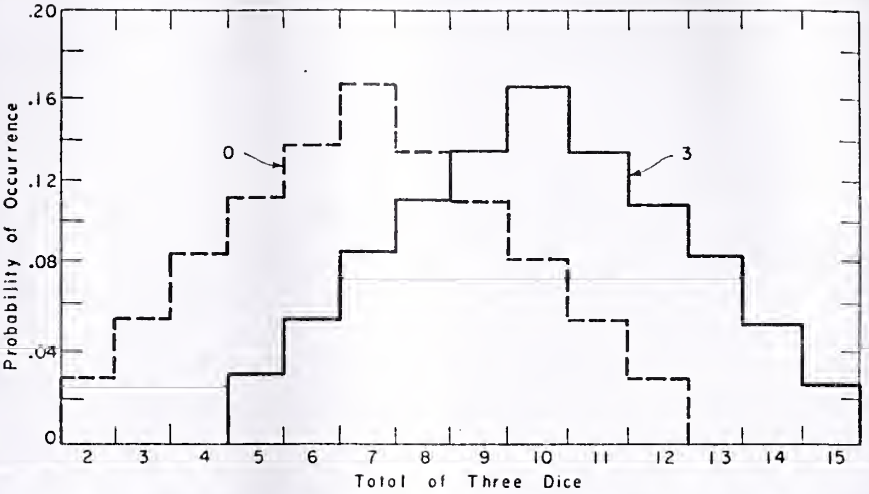


FIG. 1. The probability distributions for the dice game.

Figure 7 (from Swets, Tanner and Birdsall, 1961)

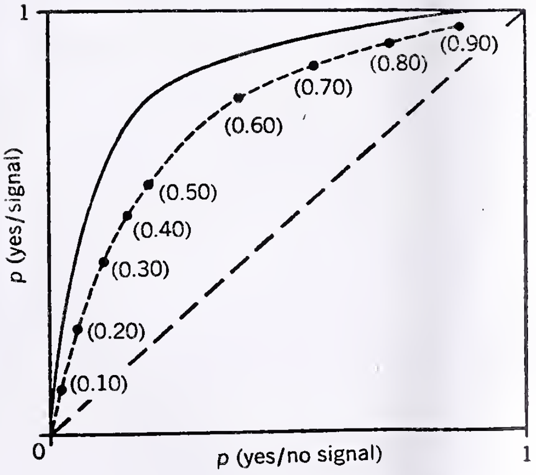


Fig. 18-16. Likelihood of correct signal detection —*p*(yes/signal)—and of false alarm—*p*(yes/no signal)—in relation to probability of signal presentation and signal intensity. Dashed curve with dots represents this relation for signal of medium intensity; numbers in parentheses are respective probabilities of signal presentation. Solid curve depicts this relation for signal of higher intensity. (From Galanter.[3])

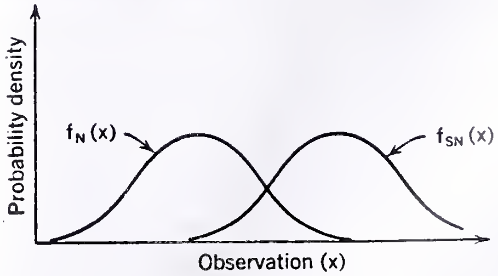


Fig. 18-17. Probability density functions of signal and signal plus noise (see text). (From Swets et al.[11])

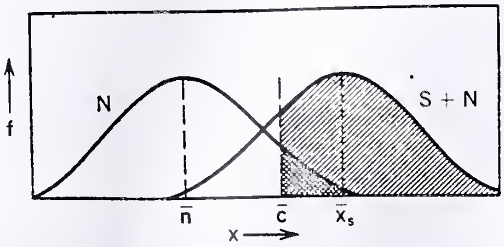


Fig. 18-18. Probability density of neural activity: *x*, for noise alone and for noise plus signal; *c* is criterion. (From Eijkman and Vendrik.[16a])

Figure 8 (from Montcastle, 1974)

Addendum

Table I	(after Collens, Nalsen and Randt, 1960 and Montcastle, 1974)
Table II	(after Whitehorn, Howe, Lessler, and Burgess, 1974 and Burgess, Howe, Lessler, and Whitehorn, 1974)

TABLE III

Conversion Table of Measurements with the Esthesiometer

Nylon Length, mm	60	55	50	45	40	35	30	25	20	15	10	5
Mean Values of Pressures in gm/sq. mm	0.96	1.08	1.16	1.40	1.84	2.40	3.20	4.60	6.64	8.84	12.84	17.68

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TABLE IV

Sample Data Sheet, Subject 1

Time, min	Voltage, v	Freq., Hz	Peak Time, ms	Peak Amplitude	Relative Amplitude, %	Threshold P_1* gm/sq. mm	Threshold P_2 gm/sq. mm
0	30	1	8.35	1978	100.0	<.96	.96
0	30	100	8.65	1770	89.5	<.96	17.68
3	↓	↓	8.70	1875	94.8	<.96	12.84
5	↓	↓	8.65	1826	92.3	<.96	>17.68
10	↓	↓	8.70	1737	87.8	<.96	12.84
15	↓	↓	8.53	1810	91.5	<.96	>17.68
20	↓	↓	8.53	1709	86.4	<.96	12.84
25	↓	↓	8.59	1772	89.5	<.96	17.68
35	0	0				<.96	.96

*P_1 = 1st phalanx P_2 = 2nd phalanx

Resistance at Recording Electrodes at time 0 min = 37 KOHM
35 min = 10 KOHM

Resistance at Stimulating Electrodes at time 0 min = 50 KOHM
35 min = 30 KOHM

Maximum Relative Decrease of Median Nerve
Action Potential = 13.6%
Occurring at time = 20 min

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TABLE V

Results of Experiment I

Subject	Max. Relative Decrease Median Nerve A.P.*,%	Time, min	Max. Relative Increase Median Nerve A.P.,%	Time, min	Max. Threshold Elevation P_2 gm/sq. mm	Time, min
1	13.6	20			>17.68	5
2	3.0	3	41.3	10	>17.68	3-25
3	3.6	0	42.2	5	>17.68	3-25
4	25.7	10	36.5	25	>17.68	15,20
5	58.4	10			>17.68	3,20
6	34.9	5			>17.68	25
7.	58.7	0			>17.68	0-25

*A.P.= action potential

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TABLE VI

Experiment 1, Latency of Median Nerve Action Potential on 100 Hz Stimulation

Subject	0 Min	25 min	Difference
1	8.65	8.59	-0.06
2	8.59	8.65	+ 0.06
3	8.76	8.94	+ 0.18
4	10.18	10.53	+ 0.35
5	8.88	9.59	+ 0.71
6	8.53	8.59	+ 0.06
7	8.47	8.59	+ 0.12
$\bar{x}$			0.25

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TABLE VII

Results of Experiment III

Subject	Maximum Threshold Variation at P2, gm/mm^2	Time, min	Maximum Threshold Variation at P3, gm/mm^2	Time, min	Return of Threshold to .96 gm/sq. mm at P_2, sec	Return of Threshold to .96 gm/sq. mm at P_2, sec
1	+2.20	5	0.00	-	95	5
2	+4.00	5	+0.44	0	10	5
3	+0.56	15,20	+0.56	5-20	5	5
4	+0.56	5,10,20	+0.56	10,15,20	5	5
5	+0.44 -0.24	10 15,20	-0.24	10	5	7
6	-0.56	5	+0.44	15,20	15	5
7	+0.80	5,10,20	+0.44 -0.24	20 10	7	5
8	+0.44 -0.24	20 10	+1.00	5	<5	<5

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